20 times higher in lymph node cell cultures from animals exposed simultaneously to both CpG1 and CT as compared to cultures derived from animals exposed to either adjuvant alone. Thus it appears that bacterial DNA containing appropriate motifs synergizes with ADP ribosylating exotoxins such as CT as adjuvants on the skin to induce higher immune responses than to either adjuvant alone.

IN THE CLAIMS

Kindly enter the following amended claims.

1. (Amended) A method for inducing an immune response in a subject comprising:

a. pretreating an area of skin of said subject, whereby said pretreating disrupts at least the skin's stratum corneum but does not penetrate the skin's dermis; and

b. applying a formulation to said pretreated area, wherein said formulation comprises:

1) at least one antigen sufficient to induce an immune response against a pathogen,

2) at least one adjuvant present in an amount effective to induce said immune response to said at least one antigen, and

3) a pharmaceutically acceptable carrier, wherein said pretreating enhances skin penetration by said formulation.

2. (Amended) The method of claim 1, wherein said pretreating comprises applying a chemical to said area of skin to enhance skin penetration by said formulation.

4. (Amended) The method of claim 3, wherein said patch is selected from the group consisting of an occlusive dressing, a nonocclusive dressing, a hydrogel dressing and a reservoir dressing.

7. (Amended) The method of claim 5, wherein said swab contains an alcohol or a composition containing alcohol.

8. (Amended) The method of claim 5, wherein said swab contains acetone or a composition containing acetone.

10. (Amended) The method of claim 5, wherein said swab contains a detergent or a detergent solution.

18. (Amended) The method of claim 1, wherein said pretreating comprises disrupting the surface layer of said pretreated area with a disrupting device or propellant gun.

20. (Amended) The method of claim 1, wherein said adjuvant is at least one of the members selected from the group consisting of bacterial DNA, CpG, cytokines, chemokines, tumor necrosis factor alpha, genetically altered toxins, chemically conjugated toxins, lipid A and lipopolysaccharides.

21. (Amended) The method of claim 20, wherein said immune response results in LN cell proliferation.

22. (Amended) The method of claim 20 wherein said adjuvant is a combination of at least two of the adjuvants selected from the group consisting of bacterial DNA, CpG, cytokines, chemokines, tumor necrosis factor alpha, genetically altered toxins, chemically conjugated toxins, lipid A and lipopolysaccharides.

23. (Amended) A method for inducing an immune response in a subject comprising:

a. pretreating an area of skin of said subject, whereby said pretreating disrupts at least the skin's stratum corneum but does not penetrate the skin's dermis;

b. applying an adjuvant formulation to said pretreated area, wherein said adjuvant formulation comprises:

1) at least one adjuvant present in an amount effective to promote said immune response and

2) a pharmaceutically acceptable carrier, wherein said pretreating enhances skin penetration by said adjuvant formulation; and

c. administering to said subject a separate antigen formulation comprising at least one antigen sufficient to induce an immune response against a pathogen.

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24. (Amended) The method of claim 23, wherein said separate antigen formulation is administered to said subject at a time after said applying of said adjuvant formulation to said pretreated area.

25. (Amended) The method of claim 23, wherein said separate antigen formulation is administered to said subject at a time before said applying of said adjuvant formulation to said pretreated area.

27. (Amended) The method of claim 23, wherein said separate antigen formulation is administered to said subject about simultaneously with said applying of said adjuvant formulation to said pretreated area.

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28. (Amended) A method for inducing an immune response in a subject comprising:

a. pretreating an area of the skin of said subject, whereby said pretreating disrupts at least the skin's stratum corneum but does not penetrate the skin's dermis;

b. applying an antigen formulation to said pretreated area, wherein said antigen formulation comprises:

1) at least one antigen sufficient to induce an immune response against a pathogen and

2) a pharmaceutically acceptable carrier, wherein said pretreating enhances skin penetration by said antigen formulation; and

c. administering to said subject a separate adjuvant formulation comprising at least one adjuvant in an amount effective to promote said immune response.

29. (Amended) The method of claim 28, wherein said separate adjuvant formulation is administered by intramuscular injection or a route selected from the group consisting of oral, buccal, nasal, rectal, vaginal and intradermal.

30. (Amended) The method of claim 28, wherein said separate adjuvant formulation is parenterally administered.

31. (Amended) The method of claim 1, wherein said antigen presents on a cell surface of a Langerhans cell to a lymphocyte, thereby inducing the immune response in the subject.

32. (Amended) The method of claim 31, wherein exposure to said adjuvant causes migration of the Langerhans cell to a lymph node.

33. (Amended) The method of claim 31, wherein exposure to said adjuvant signals the Langerhans cell to mature into a dendritic cell.

34. (Amended) The method of claim 1, wherein the antigen is derived from a bacterium.

35. (Amended) The method of claim 1, wherein the antigen is derived from a virus.

36. (Amended) The method of claim 1, wherein the antigen is derived from a fungus or a parasite or a biological warfare agent.

38. (Amended) The method of claim 1, wherein the formulation further comprises a live or an attenuated live virus or a virosome, and the at least one antigen is expressed by the live or attenuated live virus or virosome.

43 (Amended) The method of claim 1, wherein the adjuvant comprises at least one ADP-ribosylating exotoxin or a derivative thereof having adjuvant activity.

44 (Amended) The method of claim 43, wherein the ADP-ribosylating exotoxin is cholera toxin (CT).

45. (Amended) The method of claim 43, wherein the ADP-ribosylating exotoxin is *E. coli* heat-labile enterotoxin (LT).

46. (Amended) The method of claim 43, wherein the ADP-ribosylating exotoxin is pertussis toxin (PT).

47. (Amended) The method of claim 43, wherein the ADP-ribosylating exotoxin is diphtheria toxin (DT).

48. (Amended) The method of claim 1, wherein the formulation comprises a mutant ADP-ribosylating exotoxin.

49. (Amended) The method of claim 1, wherein the formulation comprises an ADP-ribosylating exotoxin B subunit.

50. (Amended) The method of claim 1, wherein the formulation is a cream or gel or emulsion or ointment.

Kindly delete claims 26 and 52-59 without prejudice or disclaimer.

Kindly enter the following new claims.

60. (New) The method of claim 1, wherein the formulation comprises an ADP-ribosylating exotoxin derivative which is less toxic but remains immunogenic.

61. (New) The method of claim 1, wherein the formulation comprises a genetically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

62. (New) The method of claim 1, wherein the formulation comprises a chemically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

63. (New) The method of claim 1, wherein the formulation comprises a genetic mutant of *E. coli* heat-labile enterotoxin.

64. (New) The method of claim 1, wherein the formulation is comprised of antigen molecules as chemical or recombinant conjugates.

65. (New) The method of claim 1, wherein the formulation is comprised of a single molecule containing both antigen and adjuvant properties.

66. (New) The method of claim 1, wherein the formulation is comprised of at least some antigen molecules which lack adjuvant properties.

67. (New) The method of claim 1, wherein the antigen has a molecular weight greater than 500 daltons.

68. (New) The method of claim 1, wherein the antigen has a molecular weight greater than 800 daltons.

69. (New) The method of claim 1, wherein the antigen has a molecular weight greater than 1000 daltons.

70. (New) The method of claim 1, wherein the antigen is a polypeptide of greater than 500 daltons molecular weight.

71. (New) The method of claim 1, wherein the antigen is a polypeptide of greater than 800 daltons molecular weight.

72. (New) The method of claim 1, wherein the antigen is a polypeptide of greater than 1000 daltons molecular weight.

73. (New) The method of claim 1, wherein the antigen is recombinantly produced.

74. (New) The method of claim 1, wherein the antigen is chemically synthesized.

75. (New) The method of claim 1, wherein the antigen is biochemically purified.

76. (New) The method of claim 1, wherein the adjuvant is recombinantly produced.

77. (New) The method of claim 1, wherein the adjuvant is chemically synthesized.

78. (New) The method of claim 1, wherein the adjuvant is biochemically purified.

79. (New) The method of claim 1, wherein said pretreating disrupts at least the skin's epidermis.

80. (New) The method of claim 1, wherein said pretreating comprises abrading the skin with an abrasive pad.

81. (New) The method of claim 1, wherein said pretreating comprises stripping the skin with an adhesive tape.

82. (New) The method of claim 1 further comprising hydrating the area of the skin after pretreatment of the skin and before application of the formulation.

83. (New) The method of claim 1, wherein the formulation comprises a whole organism and the at least one antigen is expressed by the whole organism.

84. (New) The method of claim 1, wherein a systemic immune response is induced.

85. (New) The method of claim 1, wherein a mucosal immune response is induced.

86. (New) The method of claim 1, wherein the formulation is a solution.

87. (New) The method of claim 23, wherein said separate antigen formulation is administered by intramuscular injection or a route selected from the group consisting of oral, buccal, nasal, rectal, vaginal and intradermal.

88. (New) The method of claim 23, wherein said separate antigen formulation is parenterally administered.

89. (New) The method of claim 28, wherein said separate adjuvant formulation is administered to said subject at a time after said applying of said antigen formulation to said pretreated area.

90. (New) The method of claim 28, wherein said separate adjuvant formulation is administered to said subject at a time before said applying of said antigen formulation to said pretreated area.

91. (New) The method of claim 28, wherein said separate adjuvant formulation is administered to said subject about simultaneously with said applying of said antigen formulation to said pretreated area.

IN THE SEQUENCE LISTING

Kindly enter the attached paper and computer readable forms of the Sequence Listing.